

We claim:

1. A hybrid oligomer comprising a CRE sequence and a sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.

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2. The hybrid oligomer of Claim 1, wherein the sequence, which hybridizes to the bcl-2 pre-mRNA or mRNA, comprises at least 10 consecutive bases that are complementary to the bcl-2 pre-mRNA or mRNA.

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3. The hybrid oligomer of Claim 1, wherein the sequence that hybridizes to the bcl-2 pre-mRNA or mRNA comprises 5'-TCTCCCAGCG-3'.

4. The hybrid oligomer of Claim 1, wherein the CRE sequence comprises 5'-TGACGTCA-3'.

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5. The hybrid oligomer of Claim 4, further comprising the sequence 5'-TCTCCCAGCG-3'.

6. The hybrid oligomer of Claim 1, wherein the CRE sequence is linked to the sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.

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7. The hybrid oligomer of Claim 6, wherein the CRE sequence comprises two or more CRE consensus sequences.

8. The hybrid oligomer of Claim 7, wherein a first CRE consensus sequence is linked to a second CRE consensus sequence by one or more bases.

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9. A method of inhibiting the growth of cancer cells *in vitro* comprising contacting the cancer cells with a hybrid oligomer comprising a CRE sequence and a sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.

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10. The method of Claim 9, wherein the sequence, which hybridizes to the bcl-2 pre-mRNA or mRNA, comprises at least 10 consecutive bases that are complementary to the bcl-2 pre-mRNA or mRNA.

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11. The method of Claim 9, wherein the sequence that hybridizes to the bcl-2 pre-mRNA or mRNA comprises 5'-TCTCCCAGCG-3'.

12. The method of Claim 9, wherein the CRE sequence comprises
5 5'-TGACGTCA-3'.

13. The method of Claim 12, wherein the hybrid oligomer further comprises the sequence 5'-TCTCCCAGCG-3'.

10 14. The method of Claim 9, wherein the CRE sequence is linked to the sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.

15 15. The method of Claim 14, wherein the CRE sequence comprises two or more CRE consensus sequences.

16. The method of Claim 15, wherein a first CRE consensus sequence is linked to a second CRE consensus sequence by one or more bases.

17. The method of Claim 9, further comprising contacting the cancer cells with a
20 bcl-2 antisense oligomer.

18. The method of Claim 9, further comprising contacting the cancer cells with a CRE decoy oligomer.

25 19. The method of Claim 9, further comprising contacting the cancer cells with a bcl-2 antisense oligomer and a CRE decoy oligomer.

20. The method of Claim 9, further comprising contacting the cancer cells with one or more cancer therapeutic agents.
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21. A method of treating or preventing cancer in a human comprising administering to said human, in which such treatment or prevention is desired, a hybrid oligomer comprising a CRE sequence and a sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.
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22. The method of Claim 21, wherein the sequence, which hybridizes to the bcl-2 pre-mRNA or mRNA, comprises at least 10 consecutive bases that are complementary to the bcl-2 pre-mRNA or mRNA.

5 23. The method of Claim 21, wherein the sequence that hybridizes to the bcl-2 pre-mRNA or mRNA comprises 5'-TCTCCCAGCG-3'.

24. The method of Claim 21, wherein the CRE sequence comprises 5'-TGACGTCA-3'.

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25. The method of Claim 24, wherein the hybrid oligomer further comprises the sequence 5'-TCTCCCAGCG-3'.

26. The method of Claim 21, wherein the CRE sequence is linked to the
15 sequence that hybridizes to the bcl-2 pre-mRNA or mRNA.

27. The method of Claim 26, wherein the CRE sequence comprises two or more CRE consensus sequences.

20 28. The method of Claim 27, wherein a first CRE consensus sequence is linked to a second CRE consensus sequence by one or more bases.

29. The method of Claim 21, further comprising administering a bcl-2 antisense oligomer.

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30. The method of Claim 21, further comprising administering a CRE decoy oligomer.

31. The method of Claim 21, further comprising administering a bcl-2 antisense
30 oligomer and a CRE decoy oligomer.

32. The method of Claim 21, further comprising administering one or more cancer therapeutic agents.

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33. The method of Claim 32, wherein administration of the cancer therapeutic agent follows administration of the bcl-2 antisense oligomer and the CRE decoy oligomer.

34. The method of Claim 32, wherein administration of the cancer therapeutic agent precedes administration of the bcl-2 antisense oligomer and the CRE decoy oligomer.

35. The method of Claim 32, wherein the cancer therapeutic agent is administered concurrently with the bcl-2 antisense oligomer and the CRE decoy oligomer.

36. The method of Claim 32, wherein said cancer therapeutic agent is a chemoagent, radiotherapeutic, immunotherapeutic, cancer vaccine, anti-angiogenic agent, cytokine, gene therapeutic, or hormonal agent.

37. The method of Claim 32, wherein said cancer therapeutic agent is a chemoagent, and wherein said chemoagent is dacarbazine, docetaxel, paclitaxel, cisplatin, 5-fluorouracil, doxorubicin, etoposide, cyclophosphamide, fludarabine, irinotecan, or cytosine arabinoside (Ara-C).

38. The method of Claim 32, wherein said cancer therapeutic agent is administered at a reduced dose.

39. The method of Claim 21, wherein said administration is by oral, intravenous infusion, subcutaneous injection, intramuscular injection, topical, depo injection, implantation, time-release mode, intracavitary, intranasal, inhalation, intratumor, or intraocular administration.

40. The method of Claim 21, wherein the hybrid oligomer is administered for a period consists of 2 to 13 days.

41. The method of Claim 21, wherein the hybrid oligomer is administered for a period consists of 14 to 28 days.

42. The method of Claim 21, comprising administering 0.01 to 10 mg/kg/day of a hybrid oligomer.

43. The method of Claim 21, comprising administering 10 to 50 mg/kg/day of a hybrid oligomer.

44. A method of inhibiting the growth of cancer cells *in vitro* comprising
5 contacting the cancer cells with a bcl-2 antisense oligomer and a CRE decoy oligomer.

45. The method of Claim 44, wherein the bcl-2 antisense oligomer comprises the sequence 5'-TCTCCCAGCG-3'.

10 46. The method of Claim 44, wherein the CRE decoy oligomer comprises the sequence 5'-TGACGTCA-3'.

47. The method of Claim 44, wherein the CRE decoy oligomer comprises two or more CRE consensus sequences.

15 48. The method of Claim 44, wherein a first CRE consensus sequence is linked to a second CRE consensus sequence by one or more bases.

49. The method of Claim 44, further contacting the cancer cells with one or more
20 cancer therapeutic agents.

50. A method of treating or preventing cancer in a human comprising administering to said human, in which such treatment or prevention is desired, a bcl-2 antisense oligomer and a CRE decoy oligomer.

25 51. The method of Claim 50, wherein the bcl-2 antisense oligomer comprises the sequence 5'-TCTCCCAGCG-3'.

52. The method of Claim 50, wherein the CRE decoy oligomer comprises the
30 sequence 5'-TGACGTCA-3'.

53. The method of Claim 50, wherein the CRE decoy oligomer comprises two or more CRE consensus sequences.

54. The method of Claim 50, wherein a first CRE consensus sequence is linked to a second CRE consensus sequence by one or more bases.

55. The method of Claim 50, further comprising administering one or more
5 cancer therapeutic agents.

56. The method of Claim 55, wherein administration of the cancer therapeutic agent follows administration of the bcl-2 antisense oligomer and the CRE decoy oligomer.

10 57. The method of Claim 55, wherein administration of the cancer therapeutic agent precedes administration of the bcl-2 antisense oligomer and the CRE decoy oligomer.

58. The method of Claim 55, wherein the cancer therapeutic agent is administered concurrently with the bcl-2 antisense oligomer and the CRE decoy oligomer.
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59. The method of Claim 55, wherein said cancer therapeutic agent is a chemoagent, radiotherapeutic, immunotherapeutic, cancer vaccine, anti-angiogenic agent, cytokine, gene therapeutic, or hormonal agent.

20 60. The method of Claim 55, wherein said cancer therapeutic agent is a chemoagent, and wherein said chemoagent is dacarbazine, docetaxel, paclitaxel, cisplatin, 5-fluorouracil, doxorubicin, etoposide, cyclophosphamide, fludarabine, irinotecan or cytosine arabinoside (Ara-C).

25 61. The method of Claim 55, wherein said cancer therapeutic agent is administered at a reduced dose.

62. The method of Claim 50, wherein said administration is by oral, intravenous infusion, subcutaneous injection, intramuscular injection, topical, depo injection,
30 implantation, time-release mode, intracavitary, intranasal, inhalation, intratumor, or intraocular administration.

63. The method of Claim 50, wherein the hybrid oligomer is administered for a period consists of 2 to 13 days.
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64. The method of Claim 50, wherein the hybrid oligomer is administered for a period consists of 14 to 28 days.

5 65. The method of Claim 50, comprising administering 0.01 to 10 mg/kg/day of a hybrid oligomer.

66. The method of Claim 50, comprising administering 10 to 50 mg/kg/day of a hybrid oligomer.

10 67. A pharmaceutical composition comprising a hybrid oligomer comprising a CRE sequence and a sequence that hybridizes to the bcl-2 pre-mRNA or mRNA; and a pharmaceutically acceptable carrier.

15 68. The pharmaceutical composition of Claim 67 further comprising a bcl-2 antisense oligomer.

69. The pharmaceutical composition of Claim 67 further comprising a CRE decoy oligomer.

20 70. The pharmaceutical composition of Claim 67 further comprising a bcl-2 antisense oligomer and a CRE decoy oligomer.

25 71. A pharmaceutical composition comprising a CRE decoy oligomer and a bcl-2 antisense oligomer; and a pharmaceutically acceptable carrier.

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